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MOUSE PATHOGENIC PNEUMOCOCCI AND STREPTOCOCCI IN THE SPUTUM IN PULMONARY TUBERCULOSIS

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The classification of pneumococci on the basis of immunological reactions has led to the discovery of a number of important facts, and has changed some of our conceptions regarding the pathogenicity of this organism especially for man. The progress in classifying the streptococci also is of great interest, especially with respect to the pathogenicity of this organism. Recently, Avery and Cullen[1] have been able to divide the hemolytic streptococci into two distinct groups, from human and bovine sources, by the final hydrogen ion concentration attained in culture. Corper, Donald and Antz[2] found that in the majority of cases of pulmonary tuberculosis pneumococci and streptococci were present in the sputum, the most common pathogenic varieties being pneumococci (types II and III) and streptococci of the viridans group. A few type I pneumococci and hemolytic streptococci were found. Approximately 30% of the sputums revealed so-called pathogenic varieties of pneumococci (types I, II and III), and hemolytic and green-producing streptococci. It is noteworthy that of the pneumococci type IV was more commonly found than any other, and of the streptococci the saprophytic more commonly than others. About 37% of the 216 sputums contained no pneumococci or streptococci. Uniformly negative results were obtained from the examination of the blood during life of 216 cases of pulmonary tuberculosis. These results, with those from observations during the influenza epidemic, also on cases of pulmonary tuberculosis, led to the conclusions that organisms, especially pneumococci and streptococci, found in the sputum in pulmonary tuberculosis, ordinarily play an insignificant part in the pathogenesis of this disease. It is interesting here to note also the results of Pritchett and Stillman[3] in lobar

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[1] Jour. Exper. Med., 1919, 29, p. 215.

[2] Jour. Infect. Dis., 1919, 24, p. 496.

[3] Jour. Exper. Med., 1919, 29, p. 259.

pneumonia and influenzal bronchopneumonia. They found that, whereas usually pneumococci of types I and II are associated with over 60% of the cases of lobar pneumonia, in the bronchopneumonia complicating influenza these types are rare in comparison with types III and IV, which are found normally and commonly in the mouths of healthy persons and only occasionally in lobar pneumonia. Stillman[4] further has found that the atypical type II pneumococci also fall into a parasitic group, associated with lobar pneumonia and a saprophytic group, found in normal mouths.

Since the pneumococcus and streptococcus are both highly pathogenic to the mouse it was deemed advisable to study the sputum of cases of pulmonary tuberculosis by injecting it into mice (intraperitoneally) and culturing and typing directly from the peritoneal fluid, and then to compare these results with those previously obtained by cultural methods. For comparison, the saliva of cases of pulmonary tuberculosis and the saliva and sputum of individuals free from abnormal clinical pulmonary conditions were studied also.

The sputum was obtained after rinsing the mouth with sterile salt solution several times and was delivered into a sterile enamelware sputum cup. A carefully selected bit of sputum was then washed in several changes of sterile salt solution, a portion placed in a sterile mortar and ground up for injection in amounts of 0.05 c c and 0.5 c c diluted with salt solution for injection into mice, the other portion being examined for tubercle bacilli and for the approximate numbers of the other predominating organisms. The peritoneal fluid from the mice was examined after 48 hours or immediately after death by direct typing and by smear for culture on human blood-agar plates. The saliva was obtained after several rinsings with sterile salt solution and before injection it was filtered through sterile cheese cloth. It was injected in amounts of 0.1 c c and 1 c c intraperitoneally into mice, being studied further as in the case of the sputum. The typing of the pneumococci were all carried out with well controlled agglutinating serums tested against known typed organisms. The cultures of pneumococci used in these experiments were supplied by Dr. O. T. Avery of Rockefeller Institute for Medical Research. The determination of pneumococci as differentiated from streptococci was based on the formation of capsule in suitable surroundings and bile solubility, besides the morphology and specific agglutination.

The sputum from 57 definite cases of pulmonary tuberculosis; 29 far advanced cases, all but one open; 24 moderately advanced cases, all open; and 4 incipient cases, two open, were examined in this way by inoculation into mice and the results are given in table 1.

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[4] Ibid., p. 251.

TABLE 1

Results of the Injection of Washed Sputum of Cases of Pulmonary Tuberculosis into Mice

Classification		Tubercle Bacilli		Pneumococci to Field,* Gram Stain				Result in Mouse with 0.05 C C				Result in Mouse with 0.5 C C				Pneumococcus Type†			Streptococcus	Negative Peritoneal Fluid‡
								Not Fatal	Fatal Within			Not Fatal	Fatal Within							
		+	—	1-10	11-20	21-40	Over 40		1 Day	1-2 Days	Over 2 Days		1 Day	1-2 Days	Over 2 Days	II	III	IV		
Incipient 4 cases	Afebrile	1	3	2	1	1	0	4	0	0	0	3	0	1	0	0	0	2	0	2
Moderately advanced, 24 cases (all open cases, one died within one month)	Febrile	7	1	4	2	1	1	7	0	1	0	6	0	1	1	1	1	1	0	5
	Afebrile	9	7	4	6	1	5	12	0	2	2	5	3	7	1	3	2	8	1 Streptococcus viridans	2
Far advanced, 29 cases (all open except one, eight died within two months after examinations were made)	Febrile	18	6	12	5	4	3	20	0	1	3	14	4	6	0	2	3	9	0	10
	Afebrile	4	1	0	1	2	2	3	0	1	1	0	1	3	1	0	1	3	1 Hemolytic streptococcus with Type IV pneumococcus	0
Totals......	....	39	18	22	15	9	11	46	0	5	6	28	8	18	3	6	7	23	2	19

* High power magnification.

† No Type I pneumococci were found in this series.

‡ The peritoneal fluid in these cases proved sterile on blood agar plates.

The results noted in table 1 agree well with the results of the previous observations by directly cultivating the washed sputums in pulmonary tuberculosis. The percentage, 33% sputums (57) negative for pneumococci or streptococci by mouse inoculation agree closely with the percentage 37% sputums (216) negative for the same organisms by direct cultivation. It is noteworthy also that a small percentage (4%) of hemolytic streptococcus and streptococcus viridans was found in the sputum while the predominating organisms were pneumococci especially types III and IV, some type II but no type I. There was no relation discoverable between the virulence of the sputums for mice and the condition of the patient.

A few points not brought out in the table may be of interest. In only one case did the results from the injection of 0.05 and of 0.5 c c differ: the first gave hemolytic streptococci, the other pneumococcus IV. In all other cases the two injections checked exactly as to positive results and the type of organism in the peritoneal fluid. In eight of the far advanced cases the peritoneal fluid was sterile after injecting 0.05 c c sputum while mouse which received 0.5 c c gave pneumococcus II in one case and III in one case and IV in six cases. In four of the moderately advanced cases the peritoneal fluid was sterile after injecting the smaller amount of sputum while the 0.5 c c mouse contained pneumococcus II in one case, IV in two cases and Streptococcus viridans in one case.

In order to note what difference, if any, there may be between the organisms harbored in the sputum and saliva of cases of pulmonary tuberculosis and of normal individuals a series of injections into mice were made in the same way as in the previous experiment. The material used came from 21 normal individuals, according to all clinical and laboratory methods available free from abnormal conditions in the respiratory tract and from 10 cases of pulmonary tuberculosis. The results are given in table 2.

Table 2 reveals very little difference between the results with the sputum and saliva of normal individuals, the organisms found being pneumococcus III and IV. The 10 cases of pulmonary tuberculosis examined did not prove entirely satisfactory for comparison with the normal cases, but it is easily apparent that the organisms found in the saliva of cases of pulmonary tuberculosis are identical with those found in the sputum, and as in normal saliva pneumococci III and IV predominate.

In the 21 sputums and salivas from normal individuals nine gave concordant results, while seven revealed pneumococci in the peritoneal fluid of the mice injected with saliva but none in the mice injected with sputum, and five gave pneumococci in the mice injected with sputum and none in the mice injected with the saliva. Four of the ten cases of pulmonary tuberculosis chosen had given negative results in the previous series (table 1); and in this second series both sputum and saliva were negative. In the ten cases both sputum and saliva gave the same pneumococci in the peritoneal fluid of the injected mice in 3 cases; two gave pneumococci with the saliva and none with the sputum, and two gave pneumococci with the sputum and none with the saliva; the other five were negative with both.

TABLE 2

COMPARISON OF RESULTS OF INJECTION OF SALIVA AND SPUTUM FROM NORMAL INDIVIDUALS AND OPEN CASES OF PULMONARY TUBERCULOSIS INTO MICE

Classification	Specimen	Mouse*				Pneumococcus Type		Negative Peritoneal Fluid
		Not Fatal	Fatal Within					
			1 Day	1-2 Days	Over 2 Days	III	IV	
Normal Individuals 21	Sputum	11	7	3	0	2	12	7
	Saliva	8	9	3	1	2	14	5
Pulmonary Tuberculosis 10 Cases†	Sputum	8	1	1	0	1	4	5
	Saliva	6	2	2	0	1	4	5

* The sputum was injected in amounts of 0.05 c c and 0.5 c c, the saliva in amounts of 0.1 and 1 c c; only the larger results of the injections are recorded.

† Unfortunately four of the cases of pulmonary tuberculosis chosen had previously given negative results in the experiment recorded in table 1 and therefore these results are not valuable for comparison with the results in normal individuals but rather only for comparison of the results with sputum and saliva of the same class.

SUMMARY AND CONCLUSIONS

The organisms from the sputum of open cases of pulmonary tuberculosis obtained by intraperitoneal injection of mice are mainly pneumococci of types III and IV, and a few of type II, the types which are considered saprophytic by Pritchett and Stillman in contradistinction to the pneumococcus I and certain strains of type II. A few hemolytic streptococci and streptococcus viridans were also found in the sputum. As a whole, the organisms found in the sputum from open cases of pulmonary tuberculosis by mouse inoculation differed little from those found in the saliva of the same cases, and in the sputum and saliva of normal individuals.

These results are corroborative of previous results by direct culture methods from which it was concluded that the organisms in the sputum in pulmonary tuberculosis ordinarily play an insignificant part in the pathogenesis of this disease. As far as the presence of these organisms in the lung are concerned they are to be considered more as would their presence in any nontuberculous disease, and as indicating a condition of lowered local resistance which makes possible a saprophytic residence of such bacteria. Just why the so-called parasitic types are not found remains to be discovered, as does also the infrequent occurrence of pneumococcus pneumonia in pulmonary tuberculosis.